2...

Boddupalli et al.

Application NO.: 10/714,152

In the Claims

1. (Cancelled) 1. A method of reducing the level of C-reactive protein (CRP) in an individual subject to a CRP associated inflammatory condition, comprising administering to the individual an effective amount of a composition comprising a compound of Formula I:

wherein: R is O, S, SO, SO.², a secondary or tertiary amine, a phosphate, a phosphoester, or a substituted or unsubstituted methylene group; R.sup.1 and R.² independently are H, OH, alkyl, aryl, alkenyl, alkynyl, ether, ester, amine, amide, halogen, or sulfonyl, or jointly complete a 5- or 6-membered aliphatic or aromatic ring; R³. and R⁴. independently are H, OH, alkyl, aryl, alkenyl, alkynyl, ether, ester, amine, amide, nitro, halogen, or sulfonyl, or jointly complete a 5- or 6-membered aliphatic, aromatic or heterocyclic ring; R⁵ is H, OH, alkyl, aryl, alkenyl, alkynyl, ester, or amine; R⁶. is COOH, COOR²., CONH₂., CONH₂., CONH₃.², CONR.² R.⁸, NH₂, NHR.², NHR.², NR.²R.³, OH, or OR.⁹; R.² and R⁸ independently are alkyl, aryl, aralkyl, alkenyl, or alkynyl; R⁹ is alkyl, aralkyl, alkenyl, alkynyl, or a glucoside; n is 0 to 3; and m is 0 to 5; or individual isomer, racemic or non racemic mixture of isomers, of pharmaceutically acceptable salt or solvate thereof.

- 2. (Amended) A method of reducing the level of C-reactive protein (CRP) in an individual subject to a CRP associated inflammatory condition, comprising administering to the individual an effective amount of a composition comprising 3-(6-Hydroxy-2,7,8-trimethyl-chroman-2-yl)-propionic acid. The method of claim 1, wherein the compound is selected from the group:
 - 6-Hydroxy 2,5,7,8 tetramethyl-chroman 2 carboxylic acid;
 - 6-Hydroxy-2,5,7,8-tetramethyl-chroman-2-carboxylic acid (adamantan-2-ylmethyl)-amide;
 - 2 Hydroxymethyl 6 (6 hydroxy 2,5,7,8 tetram ethyl chroman 2 ylmethoxy) tetrahydropyran 3,4,5 triol; 3 (6 Hydroxy 2 methyl chroman 2 yl) propionic acid methyl ester;
 - 3 (6 Hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester; 3 (6 Hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid;

- 3 [8 (2 Methoxycarbonyl ethyl) 3,5,6,8 tetramethyl 1,2,3,8,9,10 hexahydropyrano[3,2 f]chromen 3 yl] propionic acid methyl ester; 3 [8 (2 Carboxy ethyl) 3,5,6,8 tetramethyl 1,2,3,8,9,10 hexahydro pyrano[3,2 f]chromen 3 yl]propionic acid;
- 3 (6 Hydroxy 2 methyl chroman 2 yl) pro-pionic acid; 3 (6 Hydroxy 2,5,7,8 tetramethyl chroman 2 yl) propionic acid;
- 3 (2,5,7,8-Tetramethyl-chroman-2-yl) propionic acid; 3 (6-Hydroxy-2,7,8-trimethyl-5-nitro-chroman-2-yl) propionic acid; 3 (6-Hydroxy-2-methyl-3,4-dihydro-2H-benzo[h]chromen-2-yl) propionic acid;
- 3 (5 Bromo 6 hydroxy 2,7,8 trimethyl chroman 2-yl)-propionic acid methyl ester;
- 3 (5-Bromo-6-hydroxy-2,7,8-trimethyl-chroman-2-yl)-propioni-c acid;
- 3 (7,8-Dihydroxy-2-methyl-chroman-2-yl)-propionic acid; and
- 6-Hydroxy-2,5,7,8-tetramethyl-chroman-2-carboxylic acid.
- 3. (Cancelled) The method of claim 1, wherein the compound is selected from the group:
 - 6-Hydroxy-2,5,7,8-tetramethyl-chroman-2-carboxylic acid (adamantan-2-ylmethyl)-amide:
 - 2 Hydroxymethyl 6 (6 hydroxy 2,5,7,8 tetram ethyl chroman 2 ylmethoxy) tetrahydropyran 3,4,5 triol;
 - 3 (6 Hydroxy 2 methyl chroman 2-yl) propionic acid methyl ester;
 - 3 [8 (2-Methoxycarbonyl-ethyl)-3,5,6,8-tetramethyl-1,2,3,8,9,10-hexahydro-pyrano[3,2-f]chromen-3 yl]-propionic acid methyl ester;
 - 3-[8 (2-Carboxy ethyl) 3,5,6,8 tetramethyl-1,2,3,8,9,10 hexahydro-pyrano[-3,2-flehromen 3-yl]propionic acid; 3 (6-Hydroxy 2-methyl-chroman 2-yl) pro-pionic acid;
 - 3 (2,5,7,8 Tetramethyl chroman 2-yl) propionic acid;
 - 3 (6 Hydroxy 2,7,8 trimethyl 5 nitro chroman 2 yl) propionic acid;
 - 3 (6 Hydroxy 2 methyl 3,4 dihydro 2H benzo[h]chromen 2 yl) propionic acid;
 - 3 (5 Brome 6 hydroxy 2,7,8 trimethyl-chroman 2 yl) propionic acid methyl ester;
 - 3 (5-Bromo-6-hydroxy-2,7,8-trimethyl-chroman-2-yl)-propionic acid; and
 - 3 (7.8 Dihydroxy 2 methyl chroman 2 vl) propionic acid.
- 4. (Cancelled) The method of claim 1, wherein the compound is selected from 3 (6 hydroxy 2,7,8 trimethylchroman 2 yl) propionic acid and 3 (6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester.
- 5. (Cancelled) The method of claim 1, wherein the compound is selected from 3 (5 brome 6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester and 3 (5 brome 6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid.

Application NO.: 10/714,152

Boddupalli et al.

6. (Amended) A method of reducing the level of an inflammatory marker in an individual subject to end-stage renal disease comprising administering to the individual a composition comprising a the compound of claim 42 in an effective amount.

- 7. (**Original**) The method of claim 6, wherein said inflammatory marker is C-reactive protein (CRP).
- 8. (Cancelled) The method of claim 6, wherein said composition comprises a compound selected from the group:
 - 6-Hydroxy-2,5,7,8-tetramethyl-chroman-2-carboxyl-ic acid; 6-Hydroxy-2,5,7,8-tetramethyl-chroman-2-carboxylic acid (adamantan-2-ylmethyl) amide;
 - 2-Hydroxymethyl-6 (6-hydroxy-2,5,7,8-tetram-ethyl-chroman-2-ylmethoxy) tetrahydropyran-3,4,5-triol; 3 (6-Hydroxy-2 methyl-chroman-2-yl) propionic acid methyl ester;
 - 3 (6 Hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester; 3 (6 Hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid;
 - 3 [8 (2 Methoxycarbonyl ethyl) 3,5,6,8 tetramethyl 1,2,3,8,9,10 hexahydropyrano[3,2 f]chromen 3 yl] propionic acid methyl ester;
 - 3-[8 (2-Carboxy ethyl) 3,5,6,8-tetramethyl 1,2,3,8,9,10-hexahydro-pyrano[-3,2-f]chromen 3-yl] propionic acid; 3-(6-Hydroxy 2-methyl chroman 2-yl) propionic acid;
 - 3 (6 Hydroxy-2,5,7,8 tetramethyl-chroman-2-yl) propionic acid; 3 (2,5,7,8 Tetramethyl-chroman-2-yl) propionic acid;
 - 3 (6-Hydroxy-2,7,8-trimethyl-5-nitro-chroman-2-yl) propionic acid; 3 (6-Hydroxy-2-methyl-3,4-dihydro-2H-benzo[h]chromen-2-yl) propionic acid;
 - 3 (5 Bromo 6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester; 3 (7,8 Dihydroxy 2 methyl chroman 2 yl) propionic acid; and 6 Hydroxy 2,5,7,8 tetramethyl chroman 2 carboxylic acid.
- 9. (Cancelled) The method of claim 6, wherein the compound is selected from 3 (6 hydroxy 2,7,8 trimethylchroman 2 yl) propionic acid and 3 (6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester.
- 10. (Cancelled) The method of claim 6, wherein the compound is selected from 3 (5 brome 6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid methyl ester and 3 (5 brome 6 hydroxy 2,7,8 trimethyl chroman 2 yl) propionic acid.
- 11. (Amended) A method for ameliorating a symptom of an inflammatory condition in an individual subject to an inflammatory condition comprising administering to the individual a the composition comprising a compound of claim 42, in an amount effective to reduce the level of an inflammatory marker associated with said inflammatory condition.
- 12. (**Original**) The method of claim 11, wherein said inflammatory marker is C-reactive protein (CRP).

4

Application NO.: 10/714,152

Boddupalli et al.

13. (**Original**) The method of claim 11, wherein said inflammatory condition is selected from the group consisting of cardiovascular inflammatory condition, respiratory inflammatory condition, sepsis, diabetes, muscle fatigue, systemic lupus erythematosis (SLE), end stage renal disease (ESRD), premenstrual syndrome (PMS), and periodontal disease.

5

- 14. (**Amended**) The method of claim 11, comprising administering to the individual a-the composition of claim 2 comprising 3 (6 hydroxy 2,7,8 trimethyl chroman 2 yl) propion ic acid methyl ester in an amount effective to reduce the level of an inflammatory marker associated with said inflammatory condition.
- 15. (**Original**) The method of claim 14, wherein said inflammatory marker is C-reactive protein (CRP).
- 16. (**Original**) The method of claim 14 wherein said inflammatory condition is selected from the group consisting of cardiovascular inflammatory condition, respiratory inflammatory condition, sepsis, diabetes, muscle fatigue, SLE, renal inflammation including ESRD, premenstrual syndrome (PMS), and periodontal disease.
- 17. (Cancelled) The method of claim 11, comprising administering to the individual a composition comprising 3 (5 brome 6 hydroxy 2,7,8 trimethyl-chroman 2-yl)—propionic acid methyl ester in an amount effective to reduce the level of an inflammatory marker associated with said inflammatory condition.
- 18. (Amended) The method of claim <u>11</u>17, wherein said inflammatory marker is C-reactive protein (CRP) or IL-6.
- 19. (Cancelled) The method of claim 17, wherein said inflammatory condition is selected from the group consisting of cardiovascular inflammatory condition, respiratory inflammatory condition, sepsis, diabetes, muscle fatigue, SLE, renal inflammation including ESRD, premenstrual syndrome (PMS), and periodontal disease.
- 20. (Amended) The method of claim 12, wherein said composition further comprises a pharmaceutically acceptable carrier.
- 21. (Cancelled) The method of claim 6, wherein said composition further comprises a pharmaceutically acceptable carrier.
- 22. (Cancelled) The method of claim 11, wherein said composition further comprises a pharmaceutically acceptable carrier